IN VITRO TRANSFORMATION OF RAT PLEURAL MESOTHELIAL CELLS BY CHRYSOTILE FIBERS AND/OR BENZO-3-4-PYRENE. M.C. Jaurand, M.J. Paterour, I. Bastie Sigeac and J. Bignon, Groupe de Recherches et d'Etudes sur les Affections Respiratoires et l'Environnement (INSERM U 139 et CNRS ERA n° 845), CHU Henri Mondor, 94010 Créteil Cedex, France

In vitro transformation of rat pleural mesothelial cells has been investigated using a two-stage model, with benzo 3-4 pyrene (BP) as initiator and chrysotile fibers as promoter. The criteria used to assess transformation were (i) the efficiency of cloning in liquid medium and (ii) altered colony morphology.

Exponentially growing cells were treated at 12th passage with 1 µg/ml BP (final DMSO concentration 0.05 %) for 48 hours. When confluent the cells were subcultured (weekly) ; following 27 subsequent passages, they were incubated with 2 µg/ml UICC A chrysotile fibers for 48 hours (BP-Ch). Controls were untreated (C) or treated with only BP (BP) or with 0.05 % DMSO followed by chrysotile (DMSO-Ch). 200 cells were plated per 60 mm dish ; classification of colonies was as follows : I, sparse criss-crossing ; II, overgrowth ; III, piling up.

The results show that the efficiency of cloning increased from 1 % at 12th passage to 35 % at 20th in treated an untreated cultures and thereafter remained nearly constant ; this was slightly lower in chrysotile treated cells than in other series. Transformed colonies were observed in every series ; the percentage of type II colonies was low until 29th passage (about 10 %). Type III was not found in untreated cultures (C), even after 40 passages ; oppositely, about 20 % type III colonies were observed in the 3 other series (BP, DMSO-Ch, BP-Ch) at the 33th passage, but the number of colonies was higher in BP treated cells than in DMSO-Ch or BP-Ch treated cells.

It could be concluded to an in vitro transformation of pleural mesothelial cells by chrysotile fibers or BP ; in these experimental conditions BP had a higher transforming potency than the fibers. In addition, chrysotile fibers did not potentiate BP activity.

FIBER SIZE AND NUMBER IN AMPHIBOLE ASBESTOS-INDUCED MESOTHELIOMA. A. Churg, B. Wiggs, Department of Pathology, University of British Columbia, Vancouver, B.C.

We analyzed fiber size and number from the lungs of 10 patients who had an amphibole asbestos-induced malignant pleural mesothelioma. Amosite was found in 10 lungs and crocidolite in 9. On average amosite fibers outnumbered crocidolite by approximately 14:1. In the 8 patients who were not long time asbestos insulators, the mean number of amosite fibers was 2.8 x 10^6 fibers/gm dry lung, and of crocidolite fibers, 0.2 x 10^6/g. Crocidolite fibers were significantly narrower than amosite fibers (mean width 0.13 vs 0.23 µ), significantly shorter (mean length 4.0 vs 5.8 µ), and had a significantly higher mean aspect (length to width) ratio (48 vs 34). Aspect ratios in general increased with increasing fiber length and decreasing fiber width, but the highest values were found for thin amosite fibers at about 13 microns length, and thin crocidolite fibers at 8 or 15 to 17 microns length; longer fibers had lower aspect ratios. Comparison with data from other asbestos exposed populations indicates that mesothelioma can be induced by relatively small numbers of amphibole fibers, and also indicates that amosite is an effective mesothelial carcinogen in humans. Comparison of our data with epidemiologic and experimental predictions of carcinogenic size ranges implies that either the carcinogenic size range is much broader than has been assumed (and, specifically, is highly unlikely to be as small as 0.05 microns width or greater than 8 microns length), or, alternately, that extraordinarily small absolute numbers of fibers in certain size ranges can induce tumors in humans.

A CASE-CONTROL STUDY OF INCIDENT MESOTHELIOMA DEATHS AMONG RAILROAD WORKERS. M.B. Schenker, E. Garshick, F.E. Speizer, Department of Internal Medicine, University of California, Davis, CA and Channing Laboratory, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA.

Recent reports have suggested that former railroad workers may have experienced clinically significant exposure to asbestos. We conducted a case-control study from March 1981 to February 1982 based on incident deaths occurring among current and former male railroad workers with $\geq$ 10 years of service and born > 1900. Cause of death was based on death certificate diagnosis and diagnoses were confirmed by review of pathologic material when possible. Cases were age matched to controls. Work histories were obtained from the Railroad Retirement Board and smoking histories from next-of-kin. Twenty incident deaths from mesothelioma occurred out of 15,000 deaths. Cases had a significantly ($p<.001$) greater history of job categories associated with work in railroad shops where steam engines had been repaired. Machinists appear to have the greatest increase in odds of developing mesothelioma. Review of historical work practices confirmed that most asbestos exposure occurred in areas of steam engine repair. A separate survey of 500 current workers provided additional data on previous asbestos exposure in the industry. Because we have collected total incident deaths for the entire period we are able to estimate the magnitude of risk of mesothelioma among current and previous railroad workers and potentially make predictions for the future.

Supported in part by Training Grant No. HL-07427 from the National Heart, Lung and Blood Institute and from the Environmental Protection Agency Grant No. R807515.

DETERMINANTS OF LUNG CANCER RISK IN CIGARETTE SMOKERS. J.M. Samet, D.R. Pathak, C.G. Humble, and B.J. Skipper, Departments of Medicine, and Family, Community, and Emergency Medicine, and the New Mexico Tumor Registry, University of New Mexico School of Medicine, Albuquerque, NM.

Although cigarette smoking has been causally associated with lung cancer, the effects of specific smoking practices have not yet been completely characterized. We have examined determinants of lung cancer risk in a population-based case-control study conducted in New Mexico, 1980-1982. The study included 521 cases and 769 age, sex, ethnicity matched controls, all interviewed in person to obtain a detailed history of cigarette smoking and information concerning other risk factors. Using multiple logistic regression, we modeled the effects of amount smoked, duration of smoking, cigarette type, and smoking cessation on lung cancer risk. In current smokers, relative risk increased exponentially with amount smoked ($p < 0.001$). While relative risk increased exponentially with duration of smoking in persons under age 65 years ($p < 0.001$), it did not do so in those 65 years and older. With regard to cigarette type, the modeling suggested protection by filter cigarettes, but the effect did not attain statistical significance. Lifelong filter smokers and smokers of both filter and nonfilter cigarettes were at lower risk than lifelong smokers of nonfilter cigarettes. In ex-smokers, the pattern of variation of relative risk with amount and duration was similar to that in the current smokers. Excluding those who had stopped for one year or less, the relative risk declined exponentially with duration of smoking cessation ($p < 0.01$). For example, the relative risk estimates, in comparison to current smokers of the same amount and duration, decline from 1.0 to 0.69, 0.33, and 0.11 with 5, 15, and 30 years of smoking cessation, respectively. These analyses confirm the strong benefits of smoking cessation and indicate possible protection from filter cigarettes. The varying effect of smoking duration with age suggests that other, unidentified factors, possibly host characteristics, interact with smoking to determine lung cancer risk.